BULLETIN OF
THE NEW YORK
ACADEMY OF MEDICINE

VOL. 11 JULY, 1935 No. 7

Symposium: Angina Pectoris, With Special Reference to Coronary Artery Disease[1]

GENERAL CONSIDERATIONS[2]

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In the time at our disposal this evening, it is manifestly impossible to give anything like a complete exposition of the part of the subject allotted to me. Therefore I will confine myself to clarifying some points of view, and to taking up briefly some of the special aspects that have interested me during the last thirty-five years.

What is "angina pectoris"? When Heberden introduced this designation he did not know the cause of the condition which he was describing. It is advisable, I believe, if the term is to be employed at all, to use it in that way. One should speak only of "angina pectoris due to ?," and when the cause, in a given case, is located, the expression "angina pectoris" should drop out. If I were asked to make a definition, I would say that "angina pectoris" is a term used to describe a pain and certain accompanying clinical phenomena, of a kind that lead one to believe that the causation lies in the cardiovascular apparatus of the thorax, this including the heart, blood vessels, and nerves.

[1] Presented before the Stated Meeting of The New York Academy of Medicine, March 7, 1935.

[2] Dedicated to Professor Anton Ghon on the occasion of his seventieth birthday anniversary.

There are many conditions that may give rise to a pain resembling, or intensifying, an already existing "angina pectoris". These conditions may be of a toxic or a weakening nature, or both. The toxic factors may be bacterial or non-bacterial in origin. Among the latter may be included such influences as tobacco, lead, metabolic disorders. The bacterial causes may be in the nature of a systemic infectious disease, or of a localized infection, such as focal infections and intoxication from the alimentary tract. Of particular interest is influenza, which at times brings about what may be called a neuromyocardial disturbance. There may be present precordial pain and discomfort, and a general feeling of weakness and fatigue, lasting even for as long as three to four years, without any evidence of myocardial insufficiency. Rheumatic fever apparently may act at times in the same way as influenza, but as it is usually accompanied by well-recognized organic changes in the myocardium and blood vessels, it will be discussed later.

Among weakening causes are obesity, anemia, malnutrition, intoxication from the intestinal tract and other organs, etc., etc. While tuberculosis may act as a sensitizing agent, it is by its weakening influence that it more commonly leads to pain in the cardiac area or to intensifying the action of another cause of such pain. Various disturbances of the nervous system may also give rise to pain resembling "angina pectoris", for example, neurocirculatory asthenia, other neuroses, worry, strain, excitement, sexual disorders. The endocrine organs play a great role, especially the thyroid gland and the ovaries. The menopause is one of the most marked sensitizers.

I can refer to but few of the various disorders in the chest, of the skin, muscles, bones, esophagus and mediastinum, that may be productive of precordial pain. It is not generally realized that diseases of the pulmonary artery may give rise to a pain resembling that due to aortic disease. Frugoni, of Rome, who has specially studied this subject, calls the "angina pectoris" due to disease of the aorta and coronary arteries, dolor pallida, and that due to the pul-

monary artery, dolor caerulea. This designation is of value in emphasizing the cyanosis of pulmonary artery disease.

Of particular interest are the pains due to affections of the intercostal nerves, the spine, the subacromial bursa, and other structures about the shoulder girdle. It is not generally known that pain due to a cervical "neuritis" or spondylitis may radiate, not only to the precordium, but as far down as the lower ribs. Pain due to subacromial bursitis often radiates to the precordium (more often, the upper part), spontaneously or on raising or rotating the arm. Such movements of the arm may be of value in making a differential diagnosis. Of similar value, is the method which I have described for the relief of pain due to disorders of the shoulder girdle, especially subacromial bursitis.

Spondylitis, intercostal neuralgia (neuritis ?) and disorders of the shoulder girdle, especially bursitis, may be present together with a real "angina pectoris," and may intensify the latter. I believe that the reason for the frequent coexistence of these conditions is that they essentially have the same origin, namely, a metabolic disturbance with or without secondary focal infections. It is interesting to note how often a subacromial bursitis will start to give pain within a short time after a coronary thrombosis has occurred. At times when pains are present in both arms, the pain in the left side is due to the "angina pectoris" and that on the right, to a subacromial bursitis. An interesting case in connection with what I have just been saying, is that of a man who came under observation suffering from ventricular extrasystoles. He also presented furunculosis of the chin. On the administration of calomel, both promptly disappeared. Somewhat later he complained of pain in the precordium, and pain in the lower ribs, on the left side. On examination, a patch of eczema was found in one palm. Pressure on the cervical spine, at Erb's point, reproduced the pains described by the patient. Following a dose of calomel, and the use of alkalis, all the symptoms disappeared.

The diaphragm, as is well known, may be the source of pain resembling "angina pectoris." The resemblance is often close, because when pain is produced by diaphragmatic disturbances, anxiety, palpitation and cardiac irregularities are apt to be present. Conditions in the diaphragm that may cause pain are hernia (especially the esophageal type), eventration, pressure upwards, tension and inflammation.

In the abdomen, many organs may be the seat of a pain resembling "angina pectoris." Of particular interest, are the stomach, gallbladder, pancreas, intestinal tract, kidneys and ovaries. I will refer only to the colon, especially the descending part and the sigmoid flexure. These frequently give rise to pains that radiate to the precordial area, and even the shoulder and upper arm. Such pains may be accompanied by anxiety, palpitation and arrhythmia. The whole gastrointestinal tract is a great sensitizer of the circulatory apparatus.

Patients suffering from valvular defects (particularly rheumatic aortic insufficiency in the adolescent period), acute or chronic pericarditis, aneurysm, or myocardial disease, may develop precordial pain with less or more radiation, but we do not refer to such pain as "angina pectoris." We simply say the patient has such and such a lesion and has pain due to it. Pain may also occur in connection with attacks of paroxysmal tachycardia even when not referable to coronary artery disease. It is not realized that calcific obstruction of the abdominal aorta may also cause a pain like "angina pectoris." It is important to remember that patients having any of the conditions just mentioned may suffer pain not due to them, but originating in one of the ways now to be described, the valvular defect or other lesion perhaps acting as a sensitizing agent.

The real usual causes of what we call "angina pectoris" are:

1. Hypertension. Here the pain is apt to have wide radiations (up to the side or back of the head), and, at least at

first, to be brought on by exercise. The pains are not apt to be associated with nausea and vomiting.

2. Atherosclerotic dilatation of the arch of the aorta, or more simply, Hodgson's disease. In such patients, there is present a dilatation of the aortic arch, marked left ventricular hypertrophy, and a ringing, at times metallic, aortic second sound. Even when the coronary arteries become narrowed or occluded, and the hypertrophy decreases, a pulsation can still be felt in the jugular notch and the second sound still shows some accentuation.

3. Diseases of the coronary arteries. The important conditions are narrowing or closure of orifices or lumens, and coronary thrombosis.

It is important to remember that patients suffering from narrowing or closure of an orifice, may develop sudden attacks like those due to fresh coronary thrombosis, including nausea and vomiting. Sudden death may occur. It is also to be noted that a fresh infarction may be found in the absence of a recent coronary thrombosis, due to gradual obliteration of a number of smaller trunks.

The lesions usually found in the coronary arteries are atherosclerosis with more or less calcification, or almost pure calcification. The role of syphilis is mainly in causing disease of the aortic wall with occlusion of orifices. Rheumatic fever may cause arteritis of the aorta and/or innominate artery, narrowing or occlusion of orifices, narrowing or closure of the coronary arteries by proliferation, or coronary thrombosis. Other infections cannot now be discussed.

4. The nerves. This is an important subject that has been too much neglected. It is important to keep in mind the pathway, and the state of the psyche.

5. Spasm, alone, or secondary to already existing lesions.

6. Combinations of various causes.

As you well know, there have been put forth a number of theories in explanation of the mechanism at play in attacks of "angina pectoris." At present the anoxemia theory is most prominent. There can be no question that anoxemia is the important factor in cases in which the pain is of coronary origin. But I believe that if one studies the subject according to the classification that I have just presented there is some truth in a number of the explanations that have been offered, but for different cases. I present the following for consideration:

In hypertension, per se, we must admit that strain on the wall of the aorta plays a role (theory of Allbutt). There is clinical evidence that in hypertension the role of the nervous system is important. In fact there are cases of hypertension that much resemble hyperthyroidism, elevation of the basal metabolism being absent, or only slight.

In Hodgson's disease, we encounter a number of factors. There is tension on the wall of the aorta because the blood pressure is always elevated (not as much as in essential hypertension, unless combined with it), there are atherosclerotic deposits in the walls, inflammatory areas and scars.

There is available evidence that such deposits in the wall of a vessel may be painful. When the coronary arteries are narrowed, anoxemia plays the main role.

In rheumatic fever we may have arteritis of the aorta, innominate and carotid arteries. There may be scars in the wall of the aorta. Under all these conditions the pain may well be due to an influence on the nervous pathway. I have published notes on areas of tenderness in rheumatic inflammation (verrucous) of the innominate and of the carotid arteries. In one case, in 1925, it was found that pressure upon one part of the innominate artery produced pain in the precordium radiating to the axilla. A few days later the patient began to experience spontaneous attacks, mainly at night. They persisted for about three weeks. For a number of years, pressure in the same location (which must have been scarred) reproduced the pain. This tenderness

first disappeared in 1933. That pressure upon diseased areas in arteries, even calcific ones, may be painful is amply shown by a study of tenderness and pains due to calcific deposits in the wall of the abdominal aorta. When the coronary arteries are narrowed, or closed (by proliferative inflammation, or thrombosis, or both), any pain is to be explained on the basis of anoxemia.

In syphilitic cases, the mechanism will depend upon whether or not coronary stenosis or closure is present. There can be little doubt that syphilitic disease of the aorta can of itself cause pain.

In the cases of narrowing or closure of the coronary arteries, due to atherosclerosis and calcification, we have every reason to explain attacks of pain on the basis of anoxemia. It must be remembered, however, that these cases may be complicated by other conditions.

After closure by a thrombus, anoxemia is again the explanation. As regards symptoms at the time of an acute thrombotic closure, we must consider as possible additional factors, secondary inflammation of the arterial wall, and dilatation above the point of closure. I have some interesting observations on tenderness of arteries, above acute obstructions, that I cannot now detail.

As regards the nerve kind of "angina pectoris," there is evidence to indicate that the nervous pathway may of itself give rise to pain (like any other nerves), or, in a given case, be one of the causes. One of the arguments that has often been brought forward against the coronary origin of "angina pectoris" has been that the symptoms may be out of all proportion to the extent and degree of the coronary artery disease present. This alone must make us think of the pathway. Earlier writers spoke of neuralgia and neuritis of the cardiac nerves. I have already referred to the influence of atherosclerotic infiltration of arterial walls, and of inflammatory processes and scars. There are definite cases in which an individual died in an attack of "angina pectoris," and no lesions were found. Here we must think of the nerves as well as of spasm.

Of great interest in this connection are the following observations:

1. Cases of what may be called "alternating gout," in which attacks of gout alternate with attacks of "angina pectoris."

2. The case of a man, now 82 years of age, first seen by me with his physician, Dr. Leopold Stieglitz, when he was 77 years old. He had an attack of "angina pectoris" lasting two days, with wide radiation. It came on with an attack of gout. Two years later, in 1932, he had another attack of gout, and again, "angina pectoris." The systolic blood pressure at the time of the second attack was 195. Later there were a couple of minor attacks. Diabetes supervened two years ago. On an anti-gout regimen, there have been no further attacks of gout or of "angina pectoris." Electrocardiographic changes were never evident. The blood pressure now is about 135.

3. An important case (which I have already noted in a publication in 1932) is the following:

About six years ago, I saw a delicate woman, 41 years of age, who was suffering from attacks of "angina pectoris" with wide radiation, these attacks being marked even at rest. She had a systolic pressure of 230 and a diastolic of 130. She was considered to be in a very serious condition, and I was called in to decide whether or not an operation should be performed upon the sympathetic nervous system. She had a murmur which was rather interesting and significant. It was a whistling murmur which was most marked to the left of the sternum low down, not heard as well at the apex, transmitted more to the right than to the left. Such a murmur is not uncommonly found in connection with calcification of the mitral ring. Such calcification to my mind signifies a metabolic disturbance of the type which is called "gout" or "calcium gout". It struck me therefore that the patient might be suffering from a metabolic disturbance.

She was treated medically, not with cardiac remedies but with bromides, alkalis by mouth, and later on, alkaline enemas (carbonate of soda). Within a week she lost the pain and was able to walk without any difficulty. When I saw her nine months afterwards I was informed there had been no pain in the cardiac area during the entire period. The blood pressure was then systolic 250 and diastolic 130.

For some time she suffered from a pain in the right side of the abdomen, due to calcific obstruction of the abdominal aorta (the easily palpable area of infiltration has been steadily increasing). At present she is suffering from attacks of cholecystitis, and has none of the old attacks for which I was consulted.

I believe that I have stated enough to demonstrate the importance of considering the nervous pathway in cases of "angina pectoris."

There is much difference of opinion as regards the occurrence of spasm in the coronary arteries. My own opinion is that there is enough evidence available to make us believe that it does occur. Part of this evidence comes from cases of Raynaud's disease. There is particularly one significant case on record of a patient who first suffered spasm of the arteries of one leg, followed by a visual disturbance (the spasm of the retinal vessels was actually observed), and then suffered a typical attack of "angina pectoris" with a fatal result. No lesions were found in the aorta and coronary arteries.

Feil has reported significant observations on patients suffering attacks of "angina pectoris," with electrocardiographic changes present only during the attacks. These taken together with the studies of Pearcy and his coworkers, make it appear that these findings may well be due to spasm. Pearcy found that ligation of the coronary arteries in dogs causes pain and electrocardiographic changes, which disappear directly after the compression is released. Significant in this connection are other studies made by Pearcy and later investigators, that distension of the hollow abdominal organs may cause cardiac irregularities and

alterations in the electrocardiogram. It is reasonable to infer that these results are brought about by spasm in the coronary arteries.

Another possibility must be considered. According to a hypothesis that I have been developing, any toxic focus may cause hyperemia, edema and even hemorrhage, in the various tissues of the body, and particularly where there has been any previous alteration. A toxic focus may cause spasm, particularly in the bile ducts and the gastrointestinal tract, and probably in arteries. Spasm, in turn, may cause hyperemia and edema in various tissues, but apparently of less intensity than that ascribable to toxic foci. It is necessary to make a careful investigation of the possible role of such changes, particularly in the pathogenesis of "angina pectoris."

I cannot take up the subject of combinations of various causes in individual cases. It is too extensive. Not only is there often more than one cause in the heart and blood vessels, but there frequently come into play the influence of disease of other organs (by way of general effects and more often through reflex action), and the state of the mind. I am tempted, however, to make a brief mention of one case, because it is so instructive. A man suffering from hypertension, complained of two kinds of pain. One, evidently an inverse radiation, was brought on only by walking. It radiated from the back over the left shoulder forward to the precordium. It often also radiated to the side of the head, occasionally the occiput. There were no accompanying clinical phenomena. The second pain had been felt for only a short time, six weeks, before consulting me. This pain, which was situated in the precordium, came on at rest, mainly following meals. It did not radiate and was accompanied by dizziness, which was considered as an equivalent to nausea and vomiting, the patient being hyposensitive to pain. Electrocardiographic changes were demonstrated. This second pain was interpreted as being due to coronary artery disease. Later the patient died with symptoms of acute coronary thrombosis. It is of particular interest that

the pain due to the hypertension, which was the severer pain, was a widely radiating one, and was not accompanied by dizziness.

The aneurysms of the heart that follow so often upon thrombosis of the coronary arteries are now receiving more of the attention that they deserve. Impressed by their frequency, I requested Dr. Paul Klemperer to furnish me with the statistics of the department of pathology of the Mount Sinai Hospital, for presentation at an address delivered at a meeting of the Johns Hopkins Medical Society, in February 1931. Of all the data which Dr. Klemperer kindly furnished me, I want simply to note that aneurysms of the anterior wall of the left ventricle were found in 38 per cent of all the patients in whom a large coronary trunk had been occluded. Clinically, there is present suggestive evidence in two-thirds of these cases of aneurysm. The methods that I have found to be of value need not be detailed, because I have described them elsewhere*.

On a number of occasions, during the last years, I have stated my conviction that atherosclerosis and thrombosis of the coronary arteries, and "angina pectoris" of nerve origin are largely of metabolic origin, and that we must stop considering patients from only the standpoint of the heart and arteries. They should be regarded as affected by a general disorder, of which the cardiac manifestations are but one evidence. This conception has always been considered correct for atherosclerosis in general. It is generally accepted to be in general dependent upon mechanical strain, and a metabolic disturbance.

The exact nature of the metabolic disturbance (or disturbances) is not known. Clinical experience leads me to believe that it is the same which underlies so-called gout—irregular and typical. I usually refer to it as "metabolic disturbance due to ?," or "goutiness." The expression "goutiness" is employed only in a clinical sense and has no reference to any chemical theory, for all studies of recent

* Proceedings of the Inter-State Post-Graduate Medical Association of North America, for 1932, page 409.

years point away from the uric acid theory of gout. It seems likely, as Murchison and others long ago claimed, that a disturbance in liver function is significant in the development of the "gouty conditions." Of importance, perhaps, is a disturbance in lipoid metabolism. On another occasion, I will give the evidence that supports such a view. I might mention an observation of importance, made by Dr. Joseph Milgram, who has kindly permitted me to cite it, in advance of his proposed publication. In a case of subacromial bursitis of the supraspinatus tendon, there was aspirated 4 to 5 c.c. of a greasy, completely ether soluble material. It proved to contain 5 per cent of calcium, and 10 per cent of cholesterol, the remainder being lipoid in nature. As you know, analyses made in cases of subacromial bursitis usually show 95 per cent of calcium, and practically no organic matter. Dr. Milgram's observation is so significant, because it was carried out in an early case.

There are many causes of disturbance of liver function. Some of the important ones are heredity, the absorption of toxic substances from the intestinal tract (due largely to improper methods of eating), and the influence of the mind, especially enforced mental activity and worry. It is my opinion, based upon clinical experience, that the development of focal infections is largely dependent upon hepatic dysfunction. I have already indicated one of the ways in which focal infections may favor the development of "angina pectoris."

One is most impressed, perhaps, by the probable metabolic origin of much of "angina pectoris" of nerve origin, and atherosclerosis and thrombosis of the coronary arteries, by a consideration of the conditions with which they are often associated. They belong largely to the disorders which often occur in "goutiness." Some of these are, eczema, urticaria and angioneurotic edema, arthropathies, bursitis, tendinitis, spondylitis, various forms of neuritis, renal calculus, hemorrhoids, asthma, gallbladder disease, furunculosis, pruritus, thrombophlebitis. Diabetes, which has always been considered to be related to the "gouty" diathesis, is not infrequently noted.

Many years ago, Allbutt made a careful study of the family histories of patients under his care in Leeds. In a paper entitled, "Series and Families of Disease," he listed the disorders which he found associated with the "angina family." They correspond, in the main, to those that I have just stated.

Because of the observations just cited, and other considerations, I decided, some years ago, to apply certain methods that had been found of value in the so-called gouty conditions, to the treatment of cases of "angina pectoris." Some of the conditions in which good results had been obtained by me are, sigmoidal spasm, gallbladder disease, spondylitis, subacromial bursitis, sinusitis, hemorrhoids, and certain cases of eczema, urticaria and pruritus.

The main parts of this method of therapy (which does not interfere with the use of other remedial agents), are the use of calomel (sometimes blue mass), the administration of alkali by mouth and rectum (enemas of carbonate of soda) and the rectal implantation of B. coli. The details of the method, and a discussion of variations of it, I must leave for another occasion. The diet is not limited a great deal, the main considerations being that food should not be rapidly ingested, and that the stomach should not be distended.

I am not sure that a complete explanation can be given of the favorable results that have been obtained, in a goodly number of the patients treated along these lines,—in some, really striking. The following suggestions are offered:

In the first place, liver function is improved, and that removes a generally toxic influence. Diminution in intestinal putrefaction increases myocardial efficiency. This is clear to anyone who has observed that patients not the subject of any cardiovascular disorder, may tire on climbing stairs, and have no difficulty after the administration of a dose of calomel. Besides, the improved condition of the intestinal tract results in a diminution or disappearance of the tendency to spasm that has so bad an influence on the circulatory system.

There is a likelihood that alkalinization and perhaps the whole method of therapy makes nerves less sensitive. Occasionally a very good result goes hand in hand with a reduction in blood pressure. There are some cases of hypertension that are apparently brought about by the absorption of toxic products from the intestines. In one case, in which a very good result was obtained, as regards pain on walking, the use of calomel, alkalis and implantation of B. coli, lowered the blood pressure from 190 to 120. At first, the patient could not walk half a block. Later he was able to walk two miles with ease. He died later suddenly (in a foreign country,—of his old coronary thrombosis?). I might note here that Dr. Louis Katz of Chicago, in his experiments on induced anoxemia, found that it required more exertion to bring on pain, when large doses of alkali were administered.

It is not at all uncommon, in cases of coronary artery disease, to find a low basal metabolism. In such cases, real results may not be obtained until thyroid therapy is instituted. This experience indicates that a further investigation is needed of the mechanism of the results obtained by total thyroidectomy and by the use of other methods, the effect of which is apparently due to reduction of the basal metabolism.

Since 1919, on a number of occasions, I have drawn attention to the probability that thrombosis in the coronary arteries occurs largely because of a general thrombotic tendency. This I have called thrombophilia. By this term is meant a tendency to thrombose, independent of any disease near the vessel, and of any preceding vascular inflammation or traumatism. Occasionally such a tendency seems to be hereditary.

The occurrence of thrombosis in the coronary arteries seems to have a relationship to the metabolic disturbance of which I have spoken, and the exact nature of which we do not know. The reason why some patients with the metabolic disturbance have a tendency to hemorrhage, and others to thrombosis, is not known. It is an important subject for study. The idea that there exists a tendency to thrombose,

and that it may have a relationship to metabolic disorders, is not new. On looking up the literature, I found that as long ago as 1883, von Recklinghausen stated that there exists an individual tendency to thrombosis, independent of any circulatory disturbance, due to such metabolic disturbances as diabetes and gout.

Much of what I have said is meant to serve as the basis of a program for the wider study of the subject of tonight's symposium, with special reference to prophylaxis. I cannot refrain from quoting from Pascal: "One often writes things that one can only prove in that one encourages the reader to think about them himself."